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Intraspinal Tumors in Children

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Thirty cases of intraspinal neoplasms occurring during the first two decades of life are reviewed. Histologic examination showed 13 of these to be astrocytomas, 6 neuroblastomas, 5 sarcomas, 3 ependymomas, 2 neurofibromas and 1 a schwannoma. Orthopedic deformities developed or worsened in 60 percent of patients surviving longer than a year after diagnosis. In five patients some form of endocrine deficiency developed after irradiation. For treatment of radiosensitive extradural malignant lesions, biopsy followed by irradiation is advocated.

SPINAL CORD TUMORS occur rarely in children but present formidable problems to neurosurgeons, orthopedists and pediatricians. Frequently, there is an error or a significant delay in diagnosis; this is often related to the association of the onset of symptoms with minor illnesses or trauma.[1-9] Morbidity is related not only to the region of the spinal cord involved and the tumor type, but also to the child's often adverse response to the treatment modalities.[7,8,10-17] Extradural malignant lesions and the intrinsic gliomas predominate in the pediatric age group, whereas in adults schwannomas and meningiomas constitute the most frequent intraspinal tumors.[1,5,7,18] The ratio of intracranial to intraspinal tumors reported in the literature varies from 20:1 to 5:1 for children—in contrast to the commonly reported 5:1 ratio for adults.[1-4,9,18,19]

Clinical Data

Between 1945 and 1978 there were 30 patients treated at the University of California, San Francisco, for intraspinal neoplasms diagnosed during the first two decades of life. Excluded from this series are patients in whom operations were not carried out and those with vascular malformations, spinal metastatic lesions from previously manifested malignant conditions and tumors associated with developmental anomalies of the bony spinal canal.

Patients ranged in age from 2 months to 17 years, averaging 8.0 years; half were younger than 7 years. Of these patients, 17 were boys and 13 were girls. Predictably, boys predominated among the patients with neuroblastomas (5:1) and astrocytomas (8:5).[20,21] Twelve tumors were thoracolumbar, eight cervical, five thoracic, three cervicothoracic, and two lumbosacral. The tumors are categorized by type and location in Table 1.

The distribution of tumor types in this series is —allowing for differences in selection criteria— quite similar to that found in other series (Table 2). It is notable, however, that in our series gliomas account for 53 percent of the tumors, which is significantly higher than their incidence in any other series and more than double their incidence in all series combined.

We found no epidermoid/dermoid or lipoma without an associated anomaly of the vertebral canal. Consistent with the observations of others

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ABBREVIATIONS USED IN TEXT

CSF = cerebrospinal fluid
CT = computerized tomography

TABLE 1.—*Tumor Location and Type, in Order of Frequency*

Location	*Type*	*Number of Cases*
Intramedullary	Astrocytomas/ mixed gliomas	13
Extradural	Neuroblastomas	6
	Sarcomas	4
	Neurofibromas	2
Intradural extramedullary	Ependymomas	3
	Schwannoma	1
Both intradural and extradural	Sarcoma	1
TOTAL		30

are our findings of a slight male predominance and a clustering of tumor occurrence in children under 2 years old and in those near 13 years.*

Symptoms, Signs and Diagnosis

The duration of symptoms before a correct diagnosis was made ranged from three weeks to four years, averaging ten months. For the extradural malignant lesions, the average duration from onset of symptoms until diagnosis was 4.5 months, as compared with 2 months for ependymomas, 15 months for astrocytomas and 2 years for neurofibromas. At least six cases (20 percent) were initially diagnosed incorrectly, with the patients' symptoms attributed in three instances to previous minor trauma.

The initial symptoms are summarized in Table 3. Whereas the most frequent complaint, pain, was about equally frequent with extradural and with intramedullary lesions, there were striking differences in the motor symptomatology between these groups: all five cases of early paraparesis and all three of sphincter disturbance occurred with extradural tumors; and with intramedullary tumors, weakness was manifested as quadriparesis, hemiparesis or monoparesis. Torticollis and scoliosis occurred exclusively with astrocytomas.

The physical signs are summarized in Table 4. Most frequently found was weakness, usually manifested as an abnormality in gait. Next most frequent were sensory changes and next were abnormalities in deep tendon reflexes.

Values of cerebrospinal fluid (CSF) protein,

*1, 2, 4, 5, 7, 9, 13, 19, 22-25

TABLE 2.—*Incidence of Spinal Cord Tumors in Children—From the Literature and in the Present Series*

Tumor Type	*Hamby 1944* Number (percent)	*Anderson & Carson 1953* Number (percent)	*Ross & Bailey 1953* Number (percent)	*Svien et al 1954* Number (percent)	*Grant & Austin 1956* Number (percent)	*Hait et al 1959* Number (percent)	*Rand & Rand 1960* Number (percent)	*Matson 1969* Number (percent)	*Banna & Gryspeet 1971* Number (percent)	*Till 1975* Number (percent)	*Fraser et al 1977* Number (percent)	*Giuffre & Di Lorenzo 1977* Number (percent)	*Boggan et al 1978* Number (percent)	*Total* Number (percent)
Gliomas	44(21)	9(43)	.....	.....	.....	.....	.....	.....	9(28)	.....	4(10)	.....	.....	187(24.3)
Astrocytomas	.....	.....	4(30)	2(5)	3(10)	3(10)	9(14)	24(18)	.....	2(3)	.....	7(13)	13(43)	.....
Ependymomas	.....	.....	1(8)	4(10)	3(10)	1(3)	8(12)	6(4)	.....	4(6)	.....	1(2)	3(10)	.....
Glioblastoma	.....	.....	.....	.....	1(3)	.....	.....	.....	.....	.....	.....	.....	.....	.....
Unclassified	.....	.....	.....	2(5)	.....	5(17)	3(5)	.....	.....	10(15)	.....	2(4)	.....	.....
Medulloblastomas	.....	.....	.....	.....	.....	.....	4(6)	4(3)	6(19)	1(1)	.....	.....	.....	15(1.9)
Meningiomas	10(5)	.....	1(8)	.....	5(17)	1(3)	2(3)	3(2)	.....	2(3)	1(2)	.....	.....	25(3.2)
Neurofibromas	23(11)	3(14)	1(8)	8(20)	3(3)	2(7)	5(8)	6(4)	2(6)	6(9)	.....	3(6)	2(7)	64(8.3)
Sarcomas	42(20)	3(14)	2(15)	5(12)	5(17)	4(13)	12(18)	18(13)	4(12)	5(7)	3(8)	7(13)	5(17)	115(14.9)
Lymphomas	9(4)	.....	.....	2(5)	1(3)	.....	.....	.....	.....	.....	2(5)	.....	.....	14(1.8)
Carcinomas	.....	.....	.....	2(5)	.....	.....	.....	.....	.....	.....	1(2)	.....	.....	3(0.4)
Neuroblastomas	6(3)	2(10)	.....	.....	2(7)	6(20)	5(8)	24(18)	8(25)	17(25)	11(28)	14(26)	6(20)	101(13.1)
Ganglioneuromas	.....	.....	.....	.....	1(3)	3(10)	1(1)	3(2)	.....	1(1)	.....	1(2)	.....	10(1.3)
Lipomas	10(5)	.....	1(8)	6(15)	.....	.....	4(6)	7(5)	.....	.....	.....	.....	.....	28(3.6)
Epidermoids or dermoids	37(17)	.....	.....	.....	.....	4(13)	2(3)	14(10)	.....	3(4)	4(10)	4(8)	.....	68(8.9)
Teratomas	.....	.....	2(15)	.....	.....	.....	1(1)	13(10)	.....	1(1)	.....	2(4)	.....	19(2.5)
Blood vessel tumors	7(3)	3(14)	1(8)	3(7)	1(3)	1(3)	2(3)	3(2)	1(3)	1(1)	1(2)	.....	.....	24(3.1)
Others	26(12)	1(5)	.....	7(17)	5(17)	.....	7(11)	9(7)	2(6)	15(22)	13(32)	12(23)	1(3)	98(12.7)
TOTALS	214	21	13	41	30	30	65	134	32	68	40	53	30	771

which was determined in 20 patients, ranged from 24 to 5,400 mg per dl, averaging 750 mg per dl. In only one patient (in whom the tumor was an extradural neurofibroma) was there a normal level of CSF protein; in 12 patients it exceeded 100 mg per dl and in four of these it was more than 1,000 mg per dl. The CSF protein level tended to be lower in the patients with intramedullary tumors, although there were notable exceptions.

CSF cytology was positive for malignant cells in two patients with ependymomas and one with an undifferentiated sarcoma having an intradural subarachnoid component.

Plain x-ray films were reviewed in 26 cases, in 10 of which no abnormalities were noted. The preoperative findings are summarized in Table 5. It is notable that five of seven patients with pedicle erosion had extradural tumors, whereas only one of the extradural lesions was associated with radiologically observed scoliosis. An increased interpediculate space was observed in four patients with astrocytomas and two with neurofibromas.

Myelography provided a definitive diagnosis in each of the 29 cases in which it was done, and in 16 patients a complete block was found. Air myelography with tomography was carried out in four cases, primarily to evaluate possible communicating cystic enlargement of the spinal cord, which was not found in this series. Computerized tomography (CT) showed a paraspinous mass in two cases and vertebral body sclerosis in another. Our recent experience suggests that CT scanning utilizing computer reconstruction into sagittal and coronal planes, magnification modes and concomitant metrizamide (Amipaque) myelography should be useful in the evaluation of intradural abnormalities. The radioisotope bone scan was positive in only one of five cases, a patient with Ewing sarcoma who also had vertebral body sclerosis observable on plain x-ray films and CT scan.

TABLE 3.—*Initial Symptoms in Order of Frequency (30 Cases)*

Symptom	*Occurrences*
Pain	
Local	14
Radicular	6
Weakness	
Paraparesis	5
Monoparesis	4
Quadriparesis	2
Hemiparesis	2
Sphincter disturbance	3
Torticollis and/or scoliosis	3
Hydrocephalus	1
Neck mass	1

TABLE 4.—*Physical Findings in Order of Frequency (30 Cases)*

Sign	*Occurrences*
Paresis	
Paraparesis	9
Monoparesis	6
Hemiparesis	2
Quadriparesis	2
Hypalgesia	
Sensory loss	10
Radicular loss	3
Patchy loss	3
Deep tendon reflex abnormality	
Hyperactive	7
Hypoactive	6
Paraspinous mass	6
Scoliosis	6
Muscle atrophy	5
Sphincter disturbance	5
Vasomotor changes	1
Horner syndrome	1

TABLE 5—*Preoperative X-ray Findings in Order of Frequency (26 Cases)*

Finding	*Occurrences*
Normal	10
Scoliosis	7
Pedicle erosion	7
Interpediculate space or canal widening	6
Soft tissue mass with calcifications	2
Chest x-ray abnormality	2
Compression fracture	1
Disk space narrowing	1
Vertebral scalloping	1
Vertebral body sclerosis	1

Pathology and Survival

Astrocytomas

Eight boys and five girls had astrocytomas. Eleven were well differentiated astrocytomas, four of them cystic; and two patients had mixed gliomas, one of which had anaplastic histologic features. The cystic tumors involved more of the spinal cord, averaging 7.5 vertebral segments as compared with an average of 3.5 segments in the cases with solid tumors. Patients with cystic tumors seemed to respond better to treatment, even when there was cervical involvement. All but one of the astrocytomas were completely intramedullary.

Eleven patients received surgical operations and irradiation, and two had surgical treatment alone. Two patients received chemotherapy in addition

to irradiation and surgical operation, without observed benefit. Two patients had local reoperations. One of these was a cordectomy to excise the remaining tumor and relieve severe paraplegic flexor spasms and chronic pain. Seven patients have survived: five male and two female. Five have been followed longer than two years, with an average survival of 7.9 years. Two of the seven survivors are fully active without clinical evidence of disease and two have minor gait problems; the patient in whom cordectomy was done is paraplegic. One of the two survivors followed less than two years has no evidence of disease; the other has a progressive paraparesis. The six patients who died of tumor progression had cervical lesions, and survived an average of six years after operation (ranging from five months to 14 years). In two patients with cervical lesions, hypothyroidism developed after surgical operation and irradiation.

Neuroblastomas

Five boys and one girl had neuroblastomas, all extradural. Three of the six had palpable paraspinous masses; in one case, a biopsy of the mass constituted the patient's operation. All of the patients were treated postoperatively with irradiation in an average dose of 4,070 rads. Three patients died. Their average duration of postoperative survival was 1.6 years. Death was caused by visceral and pulmonary metastasis, with the spinal canal free of disease. In the survivors (3 months, 1 year and 19 years since diagnosis) diagnoses were made before they attained 1 year of age, as is frequently the case with long-term survivors having neuroblastomas.[7,20,26] Elevated urinary excretion of catecholamine metabolites was found inconsistently. Showing the presence by electron microscopy of intracytoplasmic secretory granules in an undifferentated tumor of small round-cells was reliable for diagnosis.

Sarcomas

Two boys and three girls had sarcomas. Three of these tumors were undifferentiated, one was a Ewing sarcoma and one was a rhabdomyosarcoma. In the only survivor among these patients, a girl with Ewing sarcoma, the duration of follow-up is less than two years. In this patient a second exploration was done for presumed recurrence, which proved to be an epiduritis probably due to irradiation; such an occurrence has been reported by Giuffre.[19] The average duration of survival for the other four patients was 1.5 years, ranging from 6 months to 3 years, 10 months. One of these patients died of a pneumocystic pulmonary infection one year and two months after operation; the metastatic tumors in this patient had responded well to chemotherapy and there was no evidence of spinal tumor at autopsy. The other three patients died of visceral metastatic lesions, and one had cerebral metastatic spread as well. The patients with sarcomas received an average of 3,750 rads of irradiation postoperatively, and two patients also received chemotherapy.

Ependymomas and Ependymoblastoma

Two girls had ependymomas and one an ependymoblastoma in the region of the conus and cauda equina. One patient received only surgical treatment and has survived 16.5 years without evidence of disease. The other two have survived 2.7 and 9.0 years postoperatively. One patient had cerebral metastatic lesions, which were verified by operation, and two intraspinal recurrences; the metastatic lesions responded well to a second course of radiation therapy and chemotherapy with BCNU (1,3-bis[2-chloroethyl]-1-nitrosurea). In this patient evidence of hypopituitarism developed—as it did in the patient with ependymoblastoma who received neuroaxis irradiation.

Neurofibromas and Schwannoma

Two patients had neurofibromas, and one a schwannoma. The three patients with these tumors have done well, having survived three, eight and ten years without recurrent symptoms or evidence of progression even though the tumors were only partly excised (and the residual tumors irradiated).

Treatment

Surgical Therapy

Laminectomies were done in 28 patients, and a three-level hemilaminectomy in one. In one patient only a biopsy study of a paraspinous mass was done. There were no perioperative deaths. The indications for surgical reexploration were development of a cyst, inadequate first biopsy, cordectomy, tumor metastasis within the spinal canal and arachnoiditis. In one patient who had an ependymoma, four laminectomies were carried out over nine years, involving a total of 18 vertebral levels. Some additional procedures done as part of the initial management of these patients

TABLE 6.—*Orthopedic Abnormalities (30 Cases)*

Finding	*Occurrences*
Preoperative	
Scoliosis	7
Increased lumbar lordosis	2
Shorter extremity	1
Valgus ankle deformity	1
Postoperative	
Kyphoscoliosis	9
Scoliosis	6
Kyphosis	2
Contractures	2
Increased lumbar lordosis	1
Equinovarus ankle deformity	1

were lumboperitoneal shunting, thoractomy and cutaneous removal of a neurofibroma.

Radiation Therapy and Chemotherapy

Twenty-six patients in whom resections were incomplete were treated with postoperative irradiation of at least 1,000 rads tumor dose, usually given through a single posterior portal.[27] Irradiation, in an average total dose of 4,000 rads per patient, was used in treating 11 of the astrocytomas, all of the neuroblastomas and sarcomas, 2 of the 3 ependymomas, 1 neurofibroma and the schwannoma. The patient with ependymoblastoma and one patient with ependymoma, in whom cerebral metastatic lesions developed, received whole-brain irradiation as well, and the latter also received local irradiation of metastatic recurrences within the canal.

Hypopituitarism has developed in two patients. Following head irradiation, as in these cases, hypopituitarism is a recognized complication that can often be prevented by proper shielding.[15] In three patients evidence of hypothyroidism has been noted. All three had cervical tumors and received incidental radiation to the thyroid area.

Eight patients received various chemotherapeutic regimens. There was no consistent response of any tumor type to chemotherapy, although BCNU has been found quite effective against ependymomas (personal communication of Drs. Victor Levin and Charles B. Wilson, Brain Tumor Research Center, University of California, San Francisco). Chemotherapy in combination with surgical and radiation therapy has not been found better than just surgical and radiation therapy in the initial management of neuroblastoma; and the use of adjuvant chemotherapy is now reserved for disseminated disease or recurrences.[28]

Orthopedic Aspects

In 60 percent of those patients surviving longer than a year, either a new orthopedic abnormality developed or significant structural worsening occurred following treatment of their tumor. The radiologically verified preoperative and postoperative postural abnormalities observed are summarized in Table 6. Orthopedic intervention was necessary in nine cases. Of the nine patients with preoperative postural abnormalities, only one did not progress postoperatively. Of our 15 patients with postoperative abnormalities, 13 also received postoperative irradiation. In four patients, bracing or body casts were necessary; in three, tendon releases were required; in one, an anterior cervical fusion was done, which improved and arrested progression of her cervical kyphosis; and in another a severe swan-neck deformity later developed after the patient decided against surgical fusion. In two patients only moderate scoliosis developed, although one had a three-level hemilaminectomy (vertebrae T-12 through L-2) and received postoperative irradiation, and the other had four laminectomies involving a total of 18 levels, as well as radiation therapy. There was no correlation between the severity of the orthopedic deformity and either the number of vertebral segments involved at operation or the patient's age at the time of treatment. However, as Fraser and associates also found, the higher the spinal level of the laminectomy, the more severe the deformity tended to be.[13]

As noted by Boldrey and co-workers,[29] orthopedic deformity—most frequently scoliosis[2,7,25]—may be the presenting sign of a childhood spinal cord tumor. Moreover, in approximately half of all children undergoing laminectomy as a result of a spinal cord tumor, a postoperative spinal deformity develops, most frequently kyphosis or kyphoscoliosis.[5,7,8,11-13,30] The cause of these deformities remains unclear, although surgical procedures, irradiation, arachnoiditis and neuromuscular imbalances have each been implicated.[8,11,16,31-35] The patient's age, the dose and field of irradiation, the extent of surgical operation, and the location of the tumor each has variable effects on the severity of the deformity.[11,13,16,31,35]

The normal configuration of the spine results from the interaction of dynamic growth and the effect of neuromuscular and gravitational forces on spinal structures.[11,30,33,36] Any of these factors

may be affected by the tumor directly or by surgical intervention or irradiation. Surgical intervention is probably the most important factor because it can destroy the critical stabilizing elements of the spine.[7,8,11,13,30,33] When wide exposure of the canal is necessary, the technique of laminotomy and reconstruction recently described by Raimondi[14] lessens the extent of surgical interference with the normal dynamic forces and stabilizing elements of the spine. An important aspect of this treatment regimen is the provision of early bracing, orthopedic attention and physical therapy. In patients with malignant extradural lesions, the use of microsurgical biopsy may diminish the role of surgical procedures in producing postoperative spinal deformity.

Discussion

The frequent misdiagnosis of childhood spinal cord tumors emphasizes the need for suspicion when examining any child with a gait disorder, back or leg pain, focal weakness, postural abnormalities or loss of acquired sphincter control. Weakness and pain are the most common symptoms; and motor, sensory and reflex changes are the most frequent physical findings.[1,4,5,7,9,13,24] The diagnostic approach must be aggressive. Complete plain x-ray films of the spine should be made because the symptoms of cervical or thoracic tumors are not infrequently confined initially to the low back or lower extremities; and in approximately 60 percent of cases of spinal tumor, close scrutiny will show pathologic radiographic changes. Contrast myelography is the diagnostic procedure of choice. The use of CT scanning is increasing.

The role of surgical procedures in the treatment of malignant extradural spinal cord tumors of childhood can reasonably be confined to decompressive laminectomy for tissue diagnosis, followed by irradiation. One can seldom achieve a total resection of these tumors, whereas they are generally radiosensitive.[16,18,20,26,37] Orthopedic abnormalities that frequently develop following treatment are in part related to surgical resection of bony and musculotendinous spinal components.[7,8,11-13,30] Recent advances in microsurgical technique reduce the need for extensive laminectomy when taking biopsy specimens of extradural lesions.[38] Other considerations supporting this approach are that the location and extent of the tumor can be well determined by computerized tomography or myelography (or both), that these patients usually die of visceral metastatic lesions with the spinal canal free of gross tumor, and that newer chemotherapeutic agents are achieving a greater response in these neoplasms.[26,28,37,39] These considerations are supported by the reported results of Gilbert and co-workers, Rubin and associates and others treating metastatic spinal cord compression in children and adults without surgical intervention.[37,40-43]

The surgical management of intradural spinal neoplasms still requires either laminectomy or laminotomy with reconstruction—as is also true for epidural lesions that progress rapidly or progress during irradiation. In the cases with lower cervical astrocytomas, an aggressive microneurosurgical approach (as employed by Malis[44] and by Garrido and Stein[45] in treating intramedullary tumors), when combined with irradiation and chemotherapy, might improve the length and the quality of life for the patient (though this view is not verified by the results in this series or review of the literature).

With recent improvements in radiotherapy and advances in chemotherapy, the prognosis for patients with epidural malignant lesions is improving.[26,28,37,39,40,42,43] Microsurgical biopsy and irradiation of these lesions probably will replace wide laminectomy except when compression of the spinal cord is proceeding precipitously. In metastatic compression of the spinal cord in adults irradiation without surgical intervention has become the primary treatment protocol for radiosensitive tumors when the type of primary tumor is known.[40,41] This approach has been effective in the management of certain spinal neoplasms in children as well.[37,42,43]

The cases of extradural malignant lesions had the worst prognosis in our study; and when they were fatal, patients' survival after diagnosis averaged less than two years. Patients with gliomas, except those in the cervical region, did well with treatment. Even patients with cervical astrocytomas survived an average of six years following treatment. With all tumor types, spinal cord function was sufficient to allow most survivors a good quality of life if treatment was initiated early and the posttreatment orthopedic and medical problems were properly managed.

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